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US005654407A

United States Patent [19]

Boyle et al.

[11] **Patent Number:** 5,654,407[45] **Date of Patent:** Aug. 5, 1997[54] **HUMAN ANTI-TNF ANTIBODIES**[75] **Inventors:** Petra Boyle, Pinole; Gayle D. Wetzel, Martinez; Kenneth J. Lembach, Danville, all of Calif.[73] **Assignee:** Bayer Corporation, Berkeley, Calif.[21] **Appl. No.:** 435,246[22] **Filed:** May 5, 1995**Related U.S. Application Data**

[63] Continuation of Ser. No. 145,060, Oct. 29, 1993, abandoned, which is a continuation-in-part of Ser. No. 269,577, Mar. 5, 1993.

[51] **Int. Cl.⁶** C07K 16/24[52] **U.S. Cl.** 530/388.15; 424/142.1; 424/145.1; 424/158.1; 435/335; 530/388.23; 530/388.24[58] **Field of Search** 424/142.1, 145.1, 424/158.1; 435/70.21, 172.2, 335; 530/388.15, 388.23, 388.24, 389.2[56] **References Cited**
PUBLICATIONSRhein, R., "Another Sepsis Drug Down—Immunex' TNF Receptor," *Biotechnology Newswatch* Oct. 4, 1993, McGraw Hill, Publishers., pp. 2-3.Boyle et al., "A Novel Monoclonal Human IgM Autoantibody Which Binds Recombinant Human and Mouse Tumor Necrosis Factor- α ," *Cell. Immunol.* 152:556-568, 1993.Boyle et al., "The B5 Monoclonal Human Autoantibody Binds to Cell Surface TNF α on Human Lymphoid Cells and Cell Lines and Appears to Recognize a Novel Epitope," *Cell. Immunol.* 152:569-581, 1993.*Primary Examiner*—Robert D. Budens*Attorney, Agent, or Firm*—James A. Giblin[57] **ABSTRACT**

Human monoclonal antibodies (mAbs) which bind to human TNF α are disclosed. Autoantibodies of both the IgM and IgG isotypes are disclosed. A preferred human monoclonal antibody is known as B5 (F78-1A10-B5 mAb) and it binds to recombinant human TNF α (rhTNF α) in ELISA format with a titer comparable to three high affinity neutralizing mouse mAbs. It also binds to cell surface TNF α and prevents TNF α secretion by human monocyte cell lines.

12 Claims, 11 Drawing Sheets